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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/089,501	04/22/2002	Hiroyuki Saito	053466-0325	9449

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EXAMINER	
BURKHART, MICHAEL D	
ART UNIT	**PAPER NUMBER**
1633	

DATE MAILED: 02/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	Application No.	Applicant(s)	
	10/089,501	SAITO ET AL.	
	Examiner	Art Unit	
	Michael D. Burkhart	1633	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 19 January 2006 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires *4* months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *9-17, 27-53*.
   Claim(s) withdrawn from consideration: *1-8*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: see continuation sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____
13. ☐ Other: _____.

Continuation sheet

11. Applicant's traverse the USC 102(b) rejection over del Zoppo (U.S. Patent 5,879,677). Applicants argue that: 1) the limitation(s) of the claim preamble(s) have been ignored, as each claim is directed to a method of treating a particular disease in patients "in need thereof"; 2) the Federal Circuit, in the cited *Rapaport v. Dement,* states proper claim analysis must take into account the type of patient being treated; 3) all the animals used by del Zoppo "lacked evidence of disease" and thus cannot anticipate any of the instant claims; 4) any injury to the animals (baboons) of del Zoppo were only the result of injury, which occurs in a "short time" and is distinct from the diseases of the present claims, which occur over a longer time frame and are not mentioned by del Zoppo.

Regarding 1), the limitations of the claim preambles were not ignored, but rather addressed in the rejections. At the top of page 3 of the Final rejection of 9/19/2005, it was clearly stated that del Zoppo disclosed a method of treatment using the instant antibodies, and that the disease treated was no different than that claimed by applicants, i.e. "hypercoagulation" or thrombosis (new clot formation). See column 3, lines 22-45 of del Zoppo. Regarding 2), the cited passage is taken out of context. Further reading of the cited case reveals that the court used the language cited by applicants to distinguish between treating the sleep apnea disorder from treating secondary symptoms related to the apnea. See page 5, second column, first full ¶, and page 6, first column, second full ¶ which states "..the [count] refers to "treatment of sleep apneas" narrowly defined, and does not also include by its plain terms "treatment of symptoms of associated with sleep apneas."" Nowhere in the Final rejection was the argument made that del

Zoppo (or the other prior art) taught treatment of secondary symptoms of "hypercoagulation" or thrombosis, but rather it was clearly stated that the anticipatory antibodies treat the underlying cause of the diseases recited in the instant claims, i.e. they bind human tissue factor and prevent clot formation (see page 2, 102(b) rejection, of the Final rejection of 9/19/2005). Regarding 3), again, this statement is taken out of context. A reading of the cited column in del Zoppo reveals that the animals lacked evidence of disease prior to any protocols or treatment. This is a common (if not universal) control found in *in vivo* models or trials, and is intended to clarify and strengthen any results by removing the possibility that pre-existing disease contributed to the experimental findings. It does not mean the animals were not subsequently used in a disease model, which they clearly were in Example 2 (read the entire Example, columns 17-21). Regarding 4), there is no limitation found in the instant claims that the disease occur over any time period. Absent evidence to the contrary, and lacking a definition in the specification, a "persistant" hypercoagulable state is considered to be any blood clot, which are persistant by nature. Del Zoppo specifically mentions that the model disease (reperfusion damage) results in thrombosis (column 3, lines 38-41). Absent evidence to the contrary, this reperfusion thrombosis occurs in arterial and venous structures and was examined by del Zoppo following reperfusion damage (column 18, lines 51-60). Furthermore, thrombosis is considered a "medial thickening of the vessels", as it involves a blood clot that occludes or restricts the diameter of the blood vessel.

Applicants traverse the USC 102(b) rejection over Randolph et al (Blood, 1998). Applicants argue that: 1) Randolph does not anticipate the instant claims for the same reasons

listed above for del Zoppo; 2) Randolph relates to basic research in an *in vitro* model and does not disclose administration to patients or therapeutic uses and therefore cannot anticipate the instant claims.

Regarding 1), see the responses above to del Zoppo. Regarding 2), it was clearly stated in the Final Rejection (9/19/2005) that Randolph discloses administration and therapeutic effects of the claimed antibodies (page 4167, first column, second paragraph). Therefore, Randolph et al do not merely disclose an *in vitro* model as applicants contend, and applicants are silent as to why the *in vivo* administration of anti-TF antibodies as disclosed in Randolph et al does not anticipate the instant claims.

Applicants traverse the USC 102(e) rejection over Sato et al (U.S. patent 6,677,436). Applicants argue that: 1) the '436 patent does not qualify as prior art; 2) '436 is eligible for the safe harbor provision of U.S.C. 103(c).

Regarding 1), based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). Regarding 2), the rejection is not a U.S.C. 103 obviousness rejection, therefore the argument that the reference qualifies under 103(c) is moot. Applicants are encouraged to read the MPEP passages cited in their response (MPEP 706.02(l), underlining added for emphasis):

> "It is important to recognize that 35 U.S.C. 103(c) applies only to consideration of prior art for purposes of obviousness under 35 U.S.C. 103. <u>It does not apply to or affect subject matter which is applied in a rejection under 35 U.S.C. 102</u> or a double patenting rejection."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael D. Burkhart whose telephone number is (571) 272-2915. The examiner can normally be reached on M-F 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Examiner
Art Unit 1633

Scott D. Priebe

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER